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EXAMINER

WHISENANT, ETHAN C

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary**Application No.**

09/536,841

Applicant(s)

FAN ET AL.

Examiner

Ethan Whisenant, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-40 is/are pending in the application.
- 4a) Of the above claim(s) 3-19 and 26-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2 and 20-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

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DETAILED ACTION

1. The applicant's Response (filed 27 FEB 03) to the Office Action has been entered. Following the entry of the claim amendments, Claim(s) 2-40 is/are pending with Claims 3-19 and 26-40 withdrawn as the result of a restriction requirement. Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

35 USC § 112- 2ND PARAGRAPH

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

3. Claim(s) 22-25 is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite because the word "dideoxynucleotides" lacks proper antecedent basis in Claim 20. Please clarify.

35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) The invention was described in --

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)

35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 102/103

7. Claim(s) 20 is/are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ugozzolii et al. (1992).

Claim 20 is drawn to a set of primers for use in determining a ratio of nucleotides present at a polymorphic locus which comprises two components. To begin, the set of primers is to comprise a pair of primers which are capable of amplifying a region of dsDNA which region comprises a polymorphic locus. Finally, the set of primers is to comprise an extension primer which extension primer comprises a 3' portion complementary to a portion of the dsDNA and a 5' oligonucleotide portion which is not complementary to the dsDNA but which is complementary to a unique known sequence of an oligonucleotide tag fixed to a solid substrate, wherein the extension primer is complementary to the 3' nucleotide sequence of the polymorphic locus and wherein the last nucleotide at the 3' end of the extension primer hybridizes exactly one nucleotide before the polymorphic locus.

Ugozzolii et al. teach a set of primers comprising all of the limitations set forth in Claim 20. Admittedly, Ugozzolii et al. do not explicitly teach using their primer set to determining a ratio of nucleotides present at a polymorphic locus. However, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey , 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963).

CLAIM REJECTIONS UNDER 35 USC § 103

8. Claim(s) 2 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al. (1992) in view of Shumaker et al. (1996).

Claim 2 is drawn to an kit comprising three components. First the kit is to comprise an array comprising one or more oligo tags fixed to a solid substrate wherein each oligo tag comprises a unique known arbitrary nucleotide sequence of sufficient length to hybridize to a locus-specific tagged oligo. Next the kit is to comprise, one or more locus-specific tagged oligos which are to comprise a 5' end

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nucleotide sequence, which hybridizes to the arbitrary sequence of a corresponding oligo tag on the array, and a 3' end nucleotide sequence, complementary to a target polynucleotide sequence in a sample, wherein the last nucleotide at the 3' end of the locus-specific tagged oligo hybridizes exactly one nucleotide before a nucleotide to be queried in the target polynucleotide sequence. Finally, the kit is to comprise at least two labeled ddNTPs, each of which is distinctly labeled. Ugozzoli et al. teach a method utilizing the first two components of the kit along with radiolabeled dNTPs in order to identify specific alleles. Therefore, it can be argued that Ugozzoli et al. teach all of the limitations of Claim 2 except Ugozzoli et al. do not teach using two or more labeled ddNTPs, each of which is distinctly labeled. However, Shumaker et al. do teach using labeled ddNTPs, each of which is distinctly labeled [i.e. fluorescently labeled with fluorophores which result in different fluorescent emissions (i.e. different colors) upon excitation], see for example p.349. Shumaker et al. also teach multiplexing in an assay very similar in nature to that of Ugozzoli et al.

Note that Ugozzoli et al., while explicitly teaching the amplification and detection of only a single SNP (i.e. the two-allele polymorphism present at codon 192 of the human tyrosinase gene), these authors do teach multiplexing (i.e. the analysis of multiple samples simultaneously) and suggest that such a format could be easily automated. See, for example, the last paragraph on page 107.

In view of the previous arguments and absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to combine the process of Ugozzoli et al. with that of Shumaker et al. The motivation to make the modification recited above would have been to eliminate the need for the radionucleotides of Ugozzoli et al. thereby making the assay of Ugozzoli et al. less dangerous and less expensive to perform. Furthermore, absent an unexpected result, once the above combination was made it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to package the reagents necessary to perform the method suggested by Ugozzoli et al. in view of Shumaker et al. into a kit in order to make performing the assay suggested by Ugozzoli et al. in view of Shumaker et al. easy and convenient for laboratory personnel.

9. Claim(s) 21-24 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al. (1992) as applied against Claim 20 above and further in view of Shumaker et al. (1996), and Reed et al. [US 5,459,038 (1995)].

Claim 21 is drawn to an kit comprising in a single container two components. To begin, the single container of the kit is to comprise two or more sets of primers of Claim 20 and at least two labeled ddNTPs, each of which is distinctly labeled. Ugozzoli et al. teach all of the limitations of Claim 21 except Ugozzoli et al. do not teach using two labeled ddNTPs, each of which is distinctly labeled, nor do

Ugozzoli et al. teach a kit comprising in a single container primers and ddNTP each of which is distinctly labeled. However, Shumaker et al. do teach using labeled ddNTPs, each of which is distinctly labeled (i.e. fluorescently labeled). Shumaker et al. also teach multiplexing. Meanwhile, Reed et al., teach placing all of the reagents (i.e. primers, dNTPs, polymerase) necessary to carry out a nucleic acid based assay into a single tube in order to improve quality control. See, for example, Column 19 of Reed et al. In addition, Reed et al. teach kits comprising the reagents necessary to carry out nucleic acid based assays.

Note that Ugozzoli et al., while explicitly teaching the amplification and detection of only a single SNP (i.e. the two-allele polymorphism present at codon 192 of the human tyrosinase gene) Ugozzoli et al. do teach multiplexing (i.e. the analysis of multiple samples simultaneously) and suggest that such a format could be easily automated. See, for example, the last paragraph on page 107.

Absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to combine the process of Ugozzoli et al. with that of Shumaker et al. The motivation to make the modification recited above would have been to eliminate the need for radionucleotides thereby making the assay of Ugozzoli et al. less dangerous/expensive to perform. Furthermore, once the above combination was made it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to package the reagents necessary to perform the method of Ugozzoli et al. in view of Shumaker et al. into a kit comprising single container in order to make performing the assay easy and convenient for laboratory personnel (i.e. improve quality control), as suggested by Reed et al.

Claim 22 is drawn to an kit comprising in a single container a sets of primers and ddNTPs of Claim 20 (?Claim 21?) and a solid support comprising an attached probe which probe is complementary to the 5' portion of the extension primer. As argued above against Claim 21, Ugozzoli et al. in view of Shumaker et al. and Reed et al. reasonably suggest the kit set forth in Claim 22. Note that Ugozzoli et al. teach a solid support comprising a probe attached thereto wherein the probe is complementary to the 5' portion of the extension primer.

Claim 23 is drawn to an embodiment of Claim 22 wherein the solid support is an oligonucleotide array.

Ugozzoli et al. teach this limitation, see for example Figure 1. Note that an oligonucleotide attached to a solid support is an "oligonucleotide array".

Claim 24 is drawn to an embodiment of Claim 22 wherein solid support is bead. Shumaker et al. also teach this limitation, see for example p.347-348, under the heading "Gel-based Assay".

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10. Claim(s) 25 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al. (1992) in view of Shumaker et al. (1996) and Reed et al. [US 5,459,038 (1995)] as applied above against Claim 22 and further in view of Mitsuhashi et al. [US 6,251,247 (2001)].

Claim 25 is drawn to an embodiment of Claim 22 wherein solid support is a microtiter plate.

Ugozzoli et al. in view of Shumaker et al. (1996) and Reed et al. teach all of the limitations of Claim 25 except these authors do not teach using a microtiter plate as a solid support. However, as evidenced by Mitsuhashi et al. the use of microtiter plates as a solid support for oligonucleotides in nucleic acid based assays was well known in the art at time of the invention. The substitution of one well known reagent with known properties for a second well known reagent with known properties is routine in the art, absent an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

11. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection.

CONCLUSION

12. Claim(s) 2 and 20-25 is/are rejected and/or objected to for the reason(s) set forth above.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

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The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.



ETHAN WHISENANT
PRIMARY EXAMINER